AMENDMENT TO THE DRAWINGS

Amended drawing figure 13 is attached following page 21 of this paper as Replacement Sheet Figure 13.

Attachment: Replacement Sheet

REMARKS

The Office Action mailed December 31, 2008, has been reviewed and the Office's comments have been considered. Pursuant to 37 CFR§ 1.111(a)(2), Applicant respectfully submits this amendment with adoption of Examiner's suggestion for claim amendments and requests reconsideration of the rejection of the claims.

1. Claim Status

A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim remains under examination in the application, is presented with an appropriate defined status identifier. Claims 1-114 are currently pending in this Application. Current claims examined include Claims 1-8, 10-15, 20-30 and 74-78. Claims 9, 16-19, 31-73 and 79-114 have been withdrawn due to restriction of the claims. Claims 75 and 77 were canceled previously.

By this Amendment, Applicants have amended claims 1, 6, 9, 10, 13, 17, 20, 22, 23, 24, 74, 76 and 78, and cancelled claims 15, 31-73, and 79-114. Support for the claim amendments can be found throughout the specification and the original claims. Specifically for amended claim 1, support can be found in the specification, *inter alia,* at paragraph [000117], page 31. Support for amended claim 20 can be found in the specification, *inter alia,* at paragraphs [000113] and [000115], page 36, and Figure 4H. Support for amended claims 22 and 23 can be found in the specification, *inter alia,* at paragraph [000113], page 3, and Example 2. No new matter has been added by the amendments to the claims. Applicants respectfully request entry of the amended claims.

2. Specification Objections

The Office objected to the disclosure, alleging that Figure 13 does not include a SEQ ID NO for Probe P1 and the BRIEF DESCRIPTION OF THE DRAWINGS in the specification does not provide a SEQ ID NO for Probe P1.

By this amendment, Applicants have submitted a Replacement Sheet for Figure 13 that identifies Probe P1 as SEQ ID NO:1. Applicants submit that the Office is mistaken that the BRIEF DESCRIPTION OF THE DRAWINGS section of the specification does not provide a SEQ ID NO for Probe P1. In an Amendment to the Specification filed September 20, 2004, Applicants amended paragraph [00090] at page 18 under BRIEF DESCRIPTION OF THE DRAWINGS section to recite the SEQ ID NOS for Figure 13. Specifically, the amended text reads "FIGURE 13 presents a map of representative probes, primers, and tether oligonucleotides for binary immuno-SDA (see SEQ ID NOS 19, 6, 10, 11, 9, 1 and 18, respectively, in order of appearance)." In addition, paragraph [00154] at page 54 was amended to identify SEQ ID NO:1 for the sequences for Probe P1. Accordingly, Applicants submit that the specification provides identification of SEQ ID NO:1 for Probe P1. No new matter has been introduced by the Replacement Sheet Figure 13, and Applicants request entry of the figure.

3. Claim Objections

The Office objected to Claim 5 because of the phrase "the hybridization blocker." Without conceding to the validity of the objection, Applicants have amended claim 5 to read "hybridization blocker oligonucleotide."

The Office objected to claim 8 because of the phrase "the length of the entire first oligonucleotide." Without conceding to the validity of the objection, Applicants have amended claim 8 to read "the length of the first oligonucleotide."

The Office objected to claim 15 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Without acquiescing to the validity of the objection, Applicants have cancelled claim 15 to further prosecution of the application. Therefore, the objection is rendered moot.

The Office objected to claim 74, allegedly due to the phrase "a 3' terminus of the second oligonucleotide" in step (ii). Without conceding to the validity of the objection, Applicants have amended claim 74 to read "the 3' terminus of the second oligonucleotide."

The Office objected to claim 78, allegedly due to the phrase "a 5' terminus of the third oligonucleotide" in step (ii). Without conceding to the validity of the objection, Applicants have amended claim 78 to read "the 5' terminus of the second oligonucleotide."

Applicants respectfully submit that the claim amendments overcome the claim objections.

4. Claim Rejections under 35 USC §112, 1st Paragraph

The Office rejected claim 76 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, alleging that the limitation "adding a splint oligonucleotide wherein a first portion of the splint oligonucleotide hybridizes with the first portion of the first oligonucleotide and a second portion of the splint oligonucleotide hybridizes with the first portion of the second oligonucleotide," which is dependent on claim 74, adds matter not disclosed in the specification.

Applicants respectfully disagree that the claim adds new matter. Nevertheless, without conceding to the validity of the rejection and merely to advance prosecution of the application, Applicants have amended claim 76 to recite the method of claim 74 further combining in step (i) a splint oligonucleotide comprising a first portion and a second portion, wherein a hybrid is formed wherein the first portion of the splint oligonucleotide hybridizes with the first portion of the first oligonucleotide and a second portion of the splint oligonucleotide hybridizes with the first portion of the second oligonucleotide. The invention is clearly described in the specification, *inter alia*, at paragraph [00098] on page 24, Figures 2A-2C, paragraph [000118] on page 37, and Figures 5A-5B. Applicants submit that amended claim 76 complies with the written description requirement, and request withdrawal of the rejection.

5. Claim Rejections under 35 USC §112, 2nd Paragraph

The Office rejected claims 1-8, 10-15, 20-30, 74, 76, and 78 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Office rejected claim 1 in view of step (iii), allegedly due to a second oligonucleotide is capable of forming a hybrid with the first portion of the first oligonucleotide and the hybridization blocker oligonucleotide is capable of forming a hybrid with the first portion of the first oligonucleotide. In addition, the Office alleged that steps (iii) and (iv) are unclear for how an amplicon can be produced by extending the 3' terminus of the first or second oligonucleotide. Also, step (vi) was rejection in view of the phrase "wherein detection of the amplification product allows detection of the analyte." By this Amendment, Applicants have amended claim 1, which specifically claims:

A method of detecting an analyte, comprising:

(i) combining:

(a) an analyte;

(b) a first proximity member, comprising a first analyte-specific binding entity and a first oligonucleotide comprising a first portion wherein the first analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the first oligonucleotide;

(c) a second proximity member, comprising a second analyte-specific binding entity and a second oligonucleotide comprising a portion that is capable of hybridizing to the first portion of the first oligonucleotide wherein the second analyte-specific binding entity is capable of forming a complex with the analyte and is conjugated to the second oligonucleotide comprising a portion that is capable of hybridizing to the first portion of the first oligonucleotide; and

(d) a hybridization blocker oligonucleotide at a concentration in excess of the concentration of the first and second proximity members, wherein the hybridization blocker oligonucleotide comprises a portion that is capable of forming a hybrid with the first portion of the first oligonucleotide to reduce hybridization between the first and second oligonucleotides and wherein the first and/or second analyte-specific binding entity is a protein;

(ii) forming a complex comprising the analyte, the first proximity member, and the second proximity member, and the hybridization blocker oligonucleotide that is hybridized with the first portion of the first oligonucleotide;

(iii) forming a hybrid by displacing the hybridization blocker oligonucleotide wherein the hybrid comprises the first portion of the first oligonucleotide and the portion of the second oligonucleotide, wherein the hybrid comprises a 3' terminus of the first or second oligonucleotide that may be extended;

(iv) extending the 3' terminus of the first or second oligonucleotide and producing an amplicon;

(v) amplifying the amplicon and producing an amplification product; and

(vi) detecting the amplification product, wherein detection of the amplification product indicates detection of the analyte.

Regarding the Office's assertion that it is unclear why an amplicon can be produced by extending the 3' terminus of the first or second oligonucleotide, Applicants submit that the

specification throughout describes producing an amplicon by extension of the oligonucleotide probes. For example, paragraph [00097] at page 22, describes two proximity members with oligonucleotide sequences P1 and P2 that hybridize, resulting in P2 with an extendable 3' end, and polymerase used to extend the 3' end of the oligonucleotide sequence to create an extension product, *i.e.*, an amplicon. This amplicon formation is depicted in Figure 1J. Accordingly, Applicants submit that the amendments to the claims render the claim definite, and request withdrawal of the rejection.

The Office rejected claim 6 as vague and indefinite. Applicants have amended claim 6 to clarify that the hybridization blocker oligonucleotide contains bases that are complementary with all of the bases of the first portion of the first oligonucleotide.

The Office rejected claim 13, alleging the claim is indefinite as to whether the double-stranded portion of the hybridization blocker oligonucleotide is capable of forming a hybrid with the first portion of the first oligonucleotide. By this Amendment, Applicants have amended claim 13 to clarify that the double-stranded portion of the hybridization blocker oligonucleotide is 3' of the portion of the hybridization blocker oligonucleotide that is capable of forming a hybrid with the first portion of the first oligonucleotide.

The Office rejected claim 20, alleging that adding a second hybridization blocker oligonucleotide that is capable of hybridizing to the portion of the second oligonucleotide does not correspond to claim 1 requiring that the portion of the second oligonucleotide is capable of forming a hybrid with the first portion of the first oligonucleotide. By this Amendment, Applicants have amended claim 20 to the method of claim 1, further comprising adding in step (i) a second hybridization blocker oligonucleotide at a concentration in excess of the concentration of the first and second proximity members, wherein the second hybridization

blocker oligonucleotide is capable of hybridizing to the portion of the second oligonucleotide wherein the portion of the second oligonucleotide is capable of forming a hybrid with the first portion of the first oligonucleotide, forming a complex in step (ii) further comprising the second hybridization blocker oligonucleotide hybridized to the portion of the second oligonucleotide, and displacing in step (iv) the second hybridization blocker oligonucleotide. Applicants submit that the amended claim is definite.

The Office rejected claim 22, alleging that it is unclear why the hybridization blocker can reduce formation of the amplicon by hybridization of the first and second oligonucleotides prior to forming a complex by a factor of at least 100-fold, as well as whether the complex in the claim is identical to the complex in step (ii) of claim 1. Applicants have amended claim 22 to the method of claim 1, wherein the hybridization blocker oligonucleotide reduces formation of the amplicon by hybridization of the first and second oligonucleotides prior to forming said complex by a factor of at least 100-fold as detected in assay relative to amplicon formation without a hybridization blocker oligonucleotide.

Similarly for the rejection of claim 23, Applicants amended the claim to the method of claim 1 wherein the hybridization blocker oligonucleotide reduces formation of the amplicon by hybridization of the first and second oligonucleotides prior to forming said complex by a factor of at least 1000-fold as detected in assay relative to amplicon formation without a hybridization blocker oligonucleotide..

The Office also rejected claim 28, alleging that claim 1 requiring that the first or second analyte-specific binding entity is a protein does not correspond with claim 28 requiring that the first or second analyte-specific binding entity is a protein complex. Applicants submit that the claims are clear and separate inventions. As detailed in the specification at paragraphs [000142]-

[000147], pages 49-51, an analyte-specific binding entity may be a protein bound to an epitope and oligonucleotide probe, or a protein complex of unlabeled antibodies bound to an epitope that are then bound to labeled antibodies bound to the oligonucleotide probe. See also Figure 10. Accordingly, claim 1 and claim 28 recite separate inventions.

The Office rejected claim 74 as vague and indefinite in view of step (iii), specifically alleging that it is unclear whether the 3' terminus is from a 3' terminus of the second oligonucleotide. Merely to advance prosecution of the application, Applicants have amended claim 74 to read "extending the 3' terminus of the second oligonucleotide and producing an amplicon.

The Office also rejected claims 74 and 78 as vague and indefinite allegedly due to step (v) requiring "wherein detection of the amplification product allows detection of the analyte." Merely to advance prosecution of the application and not agreeing with the rejection, Applicants have amended claims 74 and 78 to recite "wherein detection of the amplification product indicates detection of the analyte."

By these amendments, Applicants submit that the claims are definite, and respectfully request withdrawal of the rejections under 35 U.S.C. § 112.

6. Conclusion

In view of the above amendment, Applicants believe the pending application is in condition for allowance. Should the Examiner feel that any issues remain, Applicant request that the Examiner contact the undersigned so that the issues may be expeditiously addressed and prosecution of the instant application continue.

Applicants submit concurrently a request for a one-month extension of time under 37 C.F.R. § 1.136 and the accompanying fee, and a request for continued examination under 37 C.F.R. § 1.114. Please charge our Credit Card in the amount of $940.00 covering the fees set forth in 37 C.F.R. §§ 1.17(e) and 1.17(a)(1). In the event that any additional extension of time is necessary to prevent the abandonment of this patent application, then such extension of time is petitioned. The U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, under Order No. 020187.0208PTUS from which the undersigned is authorized to draw.

Dated: April 30, 2009

Respectfully submitted,

By _____

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Attachment: Replacement Sheet Figure 13